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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,950	03/19/2004	Christine Konradi	04843/120003	8080

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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,950	KONRADI ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *3-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/29/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, Claims 1-2 and the specific combination of nucleic acids: ATP synthase, F1 complex, O subunit; ATP synthase, F0 complex, d subunit; ATP synthase, F0 complex, c3 subunit; ATP synthase, F1 complex, gamma polypeptide 1; and ATP synthase, F0 complex, subunit F in the reply filed on 4/20/2006 is acknowledged.

2. Claims 3-38 are withdrawn from consideration.

3. An action on the merits for Claims 1-2 is set forth in the action below.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Specifically p. 24 and 26.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claim 1 is drawn to a microarray of mitochondrial energy metabolism nucleic acid molecules. Claim 2 is drawn to a microarray consisting of ATP synthase, F1 complex, O subunit; ATP synthase, F0 complex, d subunit; ATP synthase, F0 complex, c3 subunit; ATP synthase, F1 complex, gamma polypeptide 1; and ATP synthase, F0 complex, subunit F.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

Guidance in the Specification and Working Examples

The specification teaches microarrays comprising at least 2, 5, 10, 15, 20, 30, 40, 50, or 60 nuclear encoded mitochondrial energy metabolism nucleic acid molecules, or

fragments thereof, bound to a solid support, where at least 90%, 95%, or 100% of the nucleic acid molecules on the support are nuclear encoded mitodondrial energy metabolism nucleic acid molecules (p. 2). The specification does not describe by sequence identification which parts of the mitochondrial energy metabolism nucleic acid molecules are placed on the array, therefore it is unpredictable what actual sequences are placed on the array. It is unclear which parts of the gene was known at the time of the invention because the only descriptive information is genebank numbers which by themselves do not define a sequence because the sequences provided by Genebank numbers can be altered.

The specification defines "nuclear encoded mitochondrial energy metabolism nucleic acid molecule" as a polynucleotide or fragment that occurs in the nucleus and encodes a polypeptide that localizes to the mitochondria or functions in mitochondrial energy metabolism (p. 18). The specification teaches a nucleic acid microarray is composed of oligonucleotides having at least a portion of two or more nucleic acid sequences listed in Table 2 (p. 18). The specification teaches a "portion" of a fragment of a nucleic acid that is substantially identical to a reference nucleic acid (p. 19). The specification portion retains at least 50%, 75%, 80%, 90%, 95%, or even 99% of the biological activity of the referent nucleic acid (p. 19). Table 3 provides the function of the gene products encoded by these down regulated genes, their subcellular localization, and Genepept sequence identifiers (p. 30).

The specification fails to define what is encompassed by nuclear encoded mitochondrial energy metabolism nucleic acid molecule because the specification does

not describe any genes in a way in which the ordinary artisan would know which portions of the referent nucleic acid retains a specific portion of biological activity. It is unpredictable as to which parts of a sequence should be on the array since the specification provides not details as to which portions of the sequence retain the specific mitochondrial energy metabolism activity. It is unpredictable as to the actual sequences encompassed on the array because the specification only defines the sequences based on Genebank accession numbers which are not static and can be updated.

Therefore the ordinary artisan would have to do undue experimentation in order to determine which sequences are encompassed by the array. The ordinary artisan would have to determine which parts of the sequence would provide the necessary retention in activity in order to distinguish a sequence as a specific mitochondrial energy metabolism activity nucleic acid. Further the ordinary artisan is not provided with any defining characteristics of the sequences on the array except Genebank accession numbers. The ordinary artisan would have to perform undue experimentation to determine which parts of sequences should be used from a Genebank accession number that can continually be updated.

The unpredictability of the art and the state of the prior art

The state of the art teaches that there are updates to Genebank accession numbers and therefore to define a sequence solely on an accession number encompasses a large genus of potential sequence changes which is not known at the time of filing. For example, Accession No. AF047436 was submitted on 2/10/1998, but the sequence had an update to its sequence on 11/21/2002. It is unpredictable based on just the Genebank accession number which sequence was used to create the array.

It is undefined if the sequence used was the original sequence submitted or the most recently updated. It is unclear which parts of the sequence has been changed and the effect of the changes.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters that would have to be studied. To practice the invention as broadly as it is claimed, the skilled artisan would be required to produce an array without knowing which parts of the listed sequences would retain functionality. The skilled artisan would also be required to produce an array from sequences that are updated so therefore it is unpredictable if the array built by sequences on one date would be the same array built on another date. It is unclear what actual sequences the specification was in possession of at the date of filing because there is no description of the sequence provided that is not changeable.

The skilled artisan would need to perform undue experimentation to determine which parts of the sequences would be used on the array and the actual sequence of the gene on the array since the nucleic acids are defined with Accession numbers which can be updated.

To use the invention as presented would require a large amount of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus the applicants have not provided sufficient guidance to enable a skilled artisan to make the claimed invention in a manner reasonably correlated with the genus

of the claims because the genus of the claims include nucleic acid sequences that can be updated and include sequences with any number of nucleic acids. The sequences on the arrays are not defined by the specific number of nucleic acids which the sequence needs to have in order to be defined as a "functional" nuclear encoded mitochondrial energy metabolism nucleic acid molecule. Without sufficient guidance, it is unpredictable and the experimentation left to those skilled in the art is extensive. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, and the lack of guidance provided in the specification balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112-Written Description

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an isolated nucleic acid molecule comprising the sequence of SEQ ID No. 1. Claim 2 is drawn to an isolated nucleic acid molecule comprising a sequence complementary to the sequence of SEQ ID No. 1.

The claims do not describe the number or identity of nucleotides needed to be considered a nuclear encoded mitochondrial energy metabolism nucleic acid. The claims encompass nucleic acids defined by Genebank accession numbers which can be update and would therefore comprise any nucleic acid variant of any size, fragments of the sequences presented. The claims would encompass updates to the Genebank accession numbers could have variants, which include nucleotide substitutions, additions, deletions, translocations, and truncations. The specification does not describe the sequences encompassed by "nuclear encoded mitochondrial energy metabolism nucleic acid"

The claims also encompass a large genus of sequences of any size with no defining characteristics to nuclear encoded mitochondrial energy metabolism nucleic acid. An array of sequences could all be 5 mer in length and be considered as have at least 90% of the nucleic acids as nuclear encoded mitochondrial energy metabolism nucleic acid but the 5 mer nucleic acids could be any number of potential sequences.

The specification fails to describe the sequences of the mitochondrial energy metabolism nucleic acid molecules based on size. The specification depends on the description of a Genebank accession number to define the nucleic acids encompassed by the claims, but since accession numbers can be updated the specification fails to provide fixed sequences and therefore the claims include any number of possible variants.

The specification teaches that the array must include some fragment of ATP synthase, F0 complex, subunit F and point in the specification to Genebank Accession

AF047436. It is unclear, though, based solely on an accession number what constitutes an ATP synthase, F0 complex, subunit F genes sequence. Accession AF047436 has been updated since its initial submission. It is unclear which sequence, the initial or the updated, should be on the array. The specification fails to describe which nucleic acids should be placed on the array and the size of the nucleic acid sequences.

The genus of the claimed nucleic acids molecules encompasses substantial variability among the species of nucleic acids because the accession numbers, which can have enumerable updates, are the only defining characteristic of the nucleic acid molecules. The genus of the claimed invention encompasses a large variable genus of mutants, variants, and homologs from any source. The specification fails to sufficiently describe the claimed invention in clear and exact terms so that a skilled artisan would recognize that the applicants were in possession of the claimed invention at the time of filing.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids in view of the species

disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude, "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The sequences encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes

clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5474796 December 12, 1995).

Brennan teaches an array (abstract). With regard to Claim 1 and 2, Brennan teaches an array which contains oligonucleotides with 10 nucleotides each (Column 9, lines 49-50). Brennan teaches the total array represents every possible permutation of the 10-mer oligonucleotide (Column 9, lines 53-55). Therefore, Brennan teaches an array that represents 10 mer fragments of mitochondrial energy metabolism nucleic acid molecules and which would inherently include 10 mer fragments of the elected molecules.

9. Claims 1 and 2 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodor et al. (US Patent 6,582,908 June 24, 2003).

Fodor et al. teaches a number of oligonucleotides which may be used as probes in gene expression analysis (Abstract). Fodor et al. teaches nucleic acid sequences hybridize to other sequences which are their complement, once the sequence of a gene is known, probes can be designed to specifically target that gene (Column 13, lines 40-45). Fodor et al. teaches an n-mer array comprise a solid support to which are attached all possible nucleic acid sequences of a given length (Column 17, lines 24-27). Fodor et al. teaches a 2-mer array which comprises all possible oligonucleotides containing 2 base positions (Column 17, lines 27-35). Therefore, Fodor et al. teaches an array that represents 2 mer fragments and which would inherently include 2 mer fragments of the elected molecules.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Katherine Salmon 5/23/2006

Katherine Salmon
Examiner
Art Unit 1634

Jehanne Sitton

JEHANNE SITTON
PRIMARY EXAMINER

5/24/06